REMARKS/ARGUMENTS

Status of the Claims

Claims 1-3, 9-12, 17-18, 38-40, 43-46, 49-52, and 55-64 are pending in the application. Claim 19 has been canceled. Claims 1, 9, 17, and 18 have been amended. These claims have been amended to set forth that the polypeptide is pesticidal to an insect selected from the group consisting of western corn rootworm, southern corn rootworm, Colorado potato beetle, and boll weevil. Support for the amendments can be found in the specification as well as in canceled claim 19. No new matter has been added by amendment. Reexamination and reconsideration of the claims are requested in view of the following remarks.

It is noted that in the current Office Action, in the Office Action of April 17, 2008 as well as in Applicants' Response of July 11, 2008, the pending claims are listed as 1-3, 9-12, 17-19, 38, 43, 46, 49, 52, and 55-64. It is noted that Claims 39, 40, 45, 50, and 51 are also pending. Claims 39, 40, 45, 50, and 51 were objected to by the Examiner as being dependent upon a rejected base claim prior to Appeal 2007-4213. Clarification as to the status of claims 39, 40, 45, 50 and 51 with respect to the present obviousness rejection is respectfully requested. It is further requested that finality of the present office action be removed should the Examiner reject these claims to allow Applicants an opportunity to respond to any rejection of these claims.

The Rejection of the Claims Under 35 U.S.C. §103 Should Be Withdrawn

Claims 1-3, 9-12, 17-19, 38, 43, 46, 49, 52, and 55-64 were rejected under 35 USC §103(a) as being unpatentable over Michaels *et al.* (U.S. Patent No. 5,554,534 (the '534 patent)). This rejection is respectfully traversed.

The '534 patent is drawn to particular isolates of *Bacillus thuringiensis* (*Bt*) and isolated nucleotide sequences encoding δ-endotoxins. The Examiner has indicated that a nucleotide sequence encoding one such δ-endotoxin taught by the '534 patent (SEQ ID NO: 3) has 85.1% identity to SEQ ID NO:1 of the present application. The Examiner alleges that the claimed sequences would have been obvious over those disclosed within the '534 patent because one of

ordinary skill in the art would have had the motivation to produce nucleic acid molecules having 90%, 93%, 94%, or 95% identity to SEQ ID NO: 1 (of the present application) due to the suggestion by *Michaels et al.* to make variant toxins with 75% homology to the protein encoded by SEQ ID NO: 3 (Michaels' protein) and because the methods that would have been required to arrive at the claimed nucleotide sequences are routine in the art. As such, the Examiner has failed to meet the Office's burden of presenting a *prima facie* case of obviousness, which requires a showing that the art provided the motivation and teachings to make the modifications necessary to achieve the claimed polynucleotides.

The assertion by the Examiner that routine methods of identifying a claimed nucleotide sequence can render the claimed sequences obvious seems to stem from the recent *Ex parte Kubin* opinion by the Board of Patent Appeals and Interferences (BPAI), wherein the BPAI found that claims to an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO:2 were rendered obvious in light of teachings in the art that disclose an antibody that recognized the polypeptide, a nucleotide sequence encoding the mouse ortholog, and prophetic examples describing how to isolate the claimed sequences (including examples describing how the antibody could have been used to isolate the cDNA encoding the polypeptide antigen).

As Applicants have previously noted, the facts of the present case are distinguishable from *Kubin* in that the polypeptide encoded by the claimed nucleotide sequence had not been previously identified nor was the art in possession of a monoclonal antibody that could have been used to isolate a protein encoded by the claimed nucleotide sequences. The '534 patent also does not contain an example teaching how to isolate or make one of the claimed nucleotide sequences. None of the teachings in the '534 patent disclose the isolation or construction of a nucleotide sequence falling within the scope of the claims. As the '534 patent does not teach variant sequences, the prior art was not in possession of a protein that would be encoded by a nucleotide of the pending claims. Thus, the facts of the present case are not on point with *Kubin*.

Furthermore, the *Kubin* opinion is not in line with *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995), in which the Federal Circuit found that when assessing the obviousness of a biomolecule,

it is insufficient to find that the methodology for generating the biomolecule would have been obvious, but instead, it is necessary that the art render the biomolecule itself obvious. In *Kubin*, the Board claims the holdings of *Deuel* are not controlling, citing in support *KSR Int'l Co. v. Teleflex, Inc.*, 82 USPQ2d 1385 (U.S. 2007) and stating that the "obvious to try" determination of obviousness in *KSR* can be extended to the biochemical arts. Applicants note, however, that the "obvious to try" comments in *KSR* were directed to a ***combination*** of ***known*** prior art elements that would yield a predictable structure:

> "The same constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the *combination of elements* was "obvious to try." Id, at 289 (internal quotation marks omitted). When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the *known* options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a *combination* was obvious to try might show that it was obvious under 103."

Applicants respectfully submit that the facts of the present case are distinguishable over *KSR*. As noted above, the Examiner is relying on one prior art sequence not a combination of known prior art elements that would yield a predictable structure. In the present case as in *Deuel*, the claimed nucleotide sequences clearly can not be described as an obvious combination of known components.

The Examiner has asserted that one of skill in the art would have been motivated to modify SEQ ID NO: 3 of the '534 patent to generate the claimed sequences. Applicants respectfully note, however, that the Federal Circuit has indicated in *Deuel* that although structural relationships may provide a motivation to modify known compounds to obtain new compounds, in order to determine obviousness, the "*question becomes whether the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention*." *Id*, citing *In re Jones*, 958 F.2d 347, 351, 21 (Fed. Cir. 1990) and *In re Grabiak*, 769 F.2d 729, 731-32, 226 USPQ 870, 872 (Fed. Cir. 1985); emphasis added.

Applicants respectfully submit neither *Deuel*, nor its precedents, have been expressly overruled. In fact, just four weeks after the Board's opinion in *Kubin* was rendered, the Federal Circuit referred favorably to *Deuel* and reiterates that "in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007)

The Federal Circuit has recently affirmed this line of reasoning in *Eisai Co. Ltd. V. Dr. Reddy's Laboratories, Ltd. and Teva Pharmaceuticals USA, Inc.,* No. 2007-1397, 2007-1398 (Fed. Cir. 2008), which was decided after both *KSR* and *Kubin*, by finding that a chemical structure (e.g., a polynucleotide or polypeptide) can not be considered obvious unless the prior art suggests a lead compound *and modifications necessary to achieve the claimed molecule*. In *Eisai*, Teva asserted that a combination of three prior art references rendered the claims of the '552 patent to rabeprazole and its salts obvious. The prior art references teach the compound lansoprazole, which differs from rabeprazole solely in the substituent at the 4th position of the pyridine ring. Teva argued that lansoprazole would have been selected by a person of ordinary skill in the art as a lead compound that could have been modified to produce rabeprazole. The Federal Circuit found that there existed no reason to substitute the fluorinated substituent of lansoprazole for the methoxypropoxy substituent of rabeprazole. In making this conclusion, the Federal Circuit stated that "KSR presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound," (emphasis added) citing *Takeda* 492 F.3d at 1357. The Federal Circuit further states "obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e., a lead compound) in a particular way to achieve the claimed compound" *Eisai*, emphasis added.

Applicants remind the Examiner that the Court has repeatedly considered nucleic acid molecules as chemical compounds (*In re Wallach*, 378 F.3d 1330, 1335 (Fed. Cir. 2004), quoting

Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1206 (Fed. Cir. 1991)), and as such, a novel nucleic acid molecule can not be rendered obvious without identifying a reason for making the specific changes to a known nucleic acid molecule to yield a claimed nucleic acid molecule.

In the instant case, the nucleotide sequence of SEQ ID NO: 1 and the polypeptide sequence of SEQ ID NO: 2 were unknown prior to the present invention and therefore, one of ordinary skill in the art would not have had a reason to modify SEQ ID NO: 3 of the '534 patent in a manner capable of yielding a nucleic acid molecule having 90% sequence identity to SEQ ID NO: 1. Further, the '534 patent does not provide guidance or direction as to the specific modifications (e.g., nucleotide substitutions, deletions, additions) to SEQ ID NO: 3 that are necessary to yield the claimed molecules (i.e., nucleic acid molecules having 90% sequence identity to SEQ ID NO: 1). This was acknowledged by the Examiner on page 7 of the Examiner's Answer mailed March 6, 2007 at lines 15-17, which states "this sequence [SEQ ID NO: 3 of the '534 patent] can not be used as guidance for nucleic acids with 90% identity to SEQ ID NO: 1 and that encode proteins with 70% identity to SEQ ID NO: 2, as encompassed by the full scope of the claims." Accordingly, Applicants respectfully submit the '534 patent does not provide motivation or guidance to make the specific changes to SEQ ID NO: 3 of the '534 patent required to produce the claimed nucleic acid molecules.

The Examiner has further asserted that "one of ordinary skill in the art would have been motivated to make these toxins where they are pesticidal to western corn rootworm, southern corn rootworm, Colorado potato beetle, or boll weevil, given the economic impact of these pests on major crops like potato, corn, and cotton," (Office Action mailed October 24, 2008 on page 3, lines 11-14). As acknowledged by the Examiner, "SEQ ID NO: 3 of Michaels *et al.* is pesticidal for *Cyclocephala borealis* (northern masked chafer) and *Popillia japonica* (Japanese beetle)..., whereas the instant SEQ ID NO:1 is pesticidal to *Diabrotica longicornis howardi* (southern corn rootworm)" (Examiner's Answer mailed March 6, 2007 on page 7, lines 18-21). The '534 patent does not provide guidance as to how one would modify SEQ ID NO: 3 of the '534 patent, which encodes a *Bt* δ-endotoxin specific for scarab pests, to encode a polypeptide that exhibits pesticidal activity against rootworms, potato beetle, or boll weevil. Although it was known in

the art at the time of filing of the present application which domains of *Bt* toxin polypeptides are required for insect specificity (see deMaagd *et al.* (1999) *Appl. Environ. Microbiol.* 65:4369-4374), in the absence of the claimed SEQ ID NO: 1 and 2, one of ordinary skill in the art would not have known what mutations to the sequence disclosed in the '534 patent would have been required to generate sequences that encode polypeptides displaying toxicity against the rootworms, potato beetle, or boll weevil.

Applicants respectfully submit that at the time of filing, there was no reason for the skilled artisan to modify the sequence disclosed in the '534 patent in such a manner as to yield the sequences having 90% sequence identity to the instant SEQ ID NO: 1. Furthermore, there is no teaching in Michaels *et al.* as to how to modify their sequence to make it pesticidal to western corn rootworm, southern corn rootworm, Colorado potato beetle or boll weevil. Accordingly, the Examiner has failed to present a *prima facie* case of obviousness and the rejection of the claims for being obvious over the '534 patent should be withdrawn.

CONCLUSION

Accordingly, in view of the above remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If in the opinion of the Examiner a telephone conference would expedite the prosecution of the above-referenced application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required

therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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